Open bypass and endovascular procedures among diabetic foot ulcer cases in the United States from 2001 to 2010

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Objective: **The objective of this study was to evaluate trends in outcomes of inpatient mortality, surgical complications, charges, and length of stay stratified according to open vs endovascular revascularization and amputation status in patients admitted to the hospital with diabetic foot ulcers (DFUs).**

Methods: **Inpatient discharge records from the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project were used in this retrospective cohort study spanning 2001 to 2010. Multivariate regression analyses were used to simultaneously control for patient demographic and socioeconomic attributes, hospital characteristics, and comorbid case-mix disease severity.**

Results: **During the study period, 2.5 million inpatient DFU cases were observed, of which 412,051 (16.5%) involved amputation (34.8% major, 61.2% minor). Overall, 211,534 (8.5%) of DFU cases underwent revascularization (43.5% open, 51.1% endovascular treatment [EVT], 5.4% both). From 2001 vs 2010, the volume of open procedures decreased 34.9%, and EVT volume increased 197.1%. The percentage of amputations for DFUs remained relatively unchanged, and a major:minor ratio of 0.534 was observed among all cases. Across specific procedure type and amputation status, multivariate analyses indicated equal or decreased inpatient mortality and lengths of stay since 2001, and inflation-adjusted charges generally increased. The presence of a surgical complication, however, was observed to increase by >50% for open procedures involving minor amputations and >30% for open procedures involving no amputations. Because of many potential factors, surgical complications were noted to exceed approximately 900% among cases of EVT involving major amputations beginning in 2007 relative to 2001.**

Conclusions: **This nationally-representative investigation found that DFU admissions are common, long, and costly (often >$100,000 per case), with a marked shift having occurred from open bypass to EVT. Although hospital mortality and length of stay either remained the same or have decreased significantly, an increase in procedure-specific surgical complications was observed across several intervention categories. (J Vasc Surg 2014;60:1255-65.)**

Diabetic foot ulcers (DFUs) are a serious medical condition that develop in approximately one-quarter of persons with diabetes, with approximately half becoming infected and requiring hospitalization and one-fifth culminating in amputation.[1,2] The mortality rate after DFU-related amputations has been reported to exceed most malignancies, ranging from 39% to 80% after 5 years.[1,3,4] Additionally, up to one-third of all diabetes treatment costs have been attributed to the management of DFUs.[5]

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Across peripheral artery disease or ischemic limb cases overall, previous researchers have sought to investigate changes in the use of revascularization procedures at the population level over time, and reported that large increases in endovascular treatment (EVT) were coupled with decreases in open procedures in recent years.[6-10] Results of studies have suggested reductions in amputation rates and specific types of surgical complications, although other empirical analyses have reported no change in amputations over time despite the increased use of less invasive techniques.[8-10]

Only limited analyses have described either long-term patterns of revascularization among high-risk DFU cases or associated burdens of illness, particularly those that incorporated any changes in overall disease complexity that might present to inpatient settings. The purpose of this investigation was therefore to assess clinical and economic outcomes, general case-mix complexity, and use of revascularization among hospital inpatient DFU cases and associated amputations in the United States from 2001 to 2010. This study's specific objectives were to evaluate the trends in outcomes of inpatient mortality, surgical complications, charges, and length of stay (LOS), as a function of patient demographic and hospital characteristics, and comorbid disease status stratified according to open procedures vs EVT and amputation status.

METHODS

In this nationally-representative retrospective cross-sectional study, we used inpatient discharge records from the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample, a large scale dataset that generalizes to the approximately 39 million inpatient cases that occur annually in the United States.[11] A 10-year time horizon was defined from 2001 to 2010 to capture patterns of care focusing on clinical outcomes of surgical complications and inpatient mortality and economic outcomes of inflation-adjusted charges (USD, 2012) reflecting costs from the perspective of the payer and resource utilization based on LOS. Because of the anonymized nature of data within HCUP, this study was designated as exempt from Human Subjects Protection and Institutional Review Board approval.[11]

The study inclusion criteria were cases of DFUs among adults ≥18 years of age. Because no diagnosis code exists for a DFU, the validated procedure was used based on Sohn et al, wherein International Classification of Diseases, Ninth Edition (ICD-9)-Clinical Manifestation codes of diabetes (ICD-9 250.xx) in conjunction with either 707.1x (ulcer of lower limb, except pressure ulcer) or 707.9 (chronic ulcer, unspecified).[12] Open revascularization procedures were defined by ICD-9 39.25 (aorta-iliac-femoral bypass) and ICD-9 39.29 (other peripheral vascular shunt or bypass), and EVT included ICD-9 39.50 (angioplasty or atherectomy of other noncoronary vessel) and ICD-9 39.90 (insertion of non-drug-eluting peripheral vessel stent). Major amputations were defined as above ankle with ICD-9 84.13 through 84.19 (ankle disarticulation, through malleoli of tibia and fibula, below knee, of knee, above knee, hip, abdominopelvic amputation), and minor procedures involved ICD-9 84.10 to 84.12 (amputation of lower limb, toe, through foot). Peri- and postoperative surgical complications were defined to include cardiac (ICD-9 997.1: cardiac complications), perioperative stroke (997.02: iatrogenic cerebrovascular infarction or hemorrhage), respiratory (997.3 and 518.5: respiratory complications, pulmonary insufficiency after trauma and surgery), bleeding (998.1 and 285.1: hemorrhage or hematoma or seroma complicating a procedure, acute posthemorrhagic anemia), infection (998.5, 998.59, and 996.62: postoperative infection, infection due to vascular device/implant/graft), and shock (998.0: postoperative shock).

Inferential statistical analyses involved a multivariate assessment of stratified amputation and procedure categorizations that controlled for year of admission, patient socioeconomic and demographic factors (ie, age, sex, income quartile), hospital characteristics (ie, teaching status, geographic region, bed size, urban/rural location), and the Deyo-Charlson Comorbidity Index (ie, a validated measure of case-mix disease severity).[13] Stratification of analyses was undertaken using revascularization procedure type (ie, open, EVT) and amputation (ie, major, minor, none). A generalized linear model framework with maximum likelihood estimation was used, wherein the: (1) presence of a surgical complication was assessed using binomial/Bernoulli (logistic) regression; (2) total number of surgical complications was assessed using a Poisson regression with log-link; (3) charges were assessed using a gamma regression and log-link; and (4) LOS used a generalized negative binomial with log-link.[14,15] All multivariate findings were interpreted consistently as relative risk measures (eg, <1.0 indicating a reduced likelihood, =1.0 indicating no difference in likelihood, and >1.0 indicating an increased likelihood), more specifically as: odds ratios (ORs) for generalized binomial (logistic) regression; incidence rate ratios (IRRs) for Poisson and negative binomial regression; and exponentiated beta coefficient estimates for gamma regression.[15] Because of the large number of multiple comparisons drawn across the study's generalized linear model analytic subgroups, the Simes procedure was used to correct for false discovery rates, yielding a critical *P*-value of .023 for statistical significance.[16] Additionally, a Taylor-series approach was used to ensure robust and accurate standard error determination that also incorporated appropriate statistical weighting to yield nationally-representative results based on HCUP's complex survey

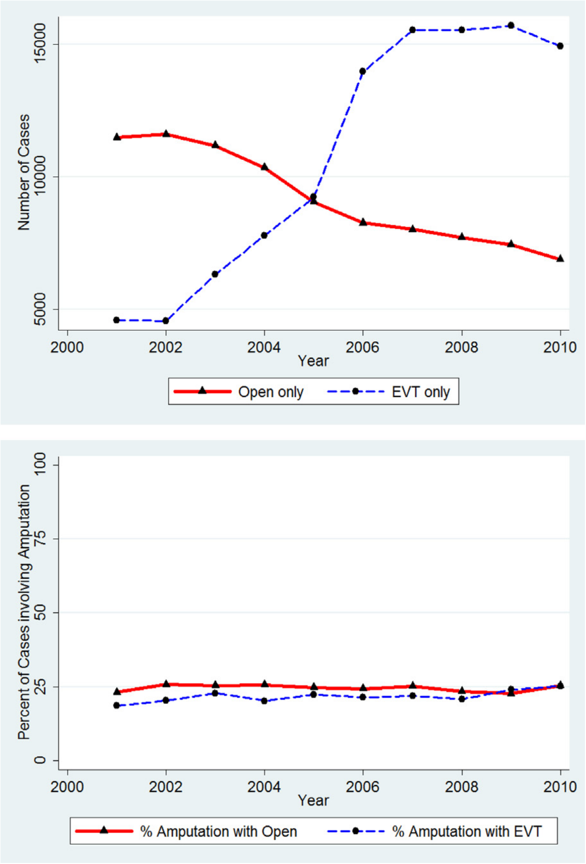

Fig. Open bypass and endovascular (*EVT*) procedures based on volume and percent involving amputation, 2001 to 2010.

Table I. Descriptive statistics, stratified according to procedure

Variable	*Open bypass procedure only (n = 92,029)*	*Endovascular procedure only (n = 108,124)*	*Open bypass with endovascular procedure, combined (n = 11,381)*	*Overall, any revascularization (N = 211,534)*
Patient characteristics				
Age	68.6 (±11.2)	68.6 (±11.9)	67.9 (±10.8)	68.6 (±11.5)
Charges (U.S., 2012)	\$90,546 (±90,355)	\$87,961 (±81,200)	\$131,116 (±107,545)	\$91,398 (±87,361)
Total national bill (U.S., 2012)	\$8.15 billion	\$9.38 billion	\$1.46 billion	\$18.99 billion
Female sex	39.6% (n = 36,425)	42.9% (n = 46,383)	40.1% (n = 4561)	41.3% (n = 87,369)
Income quartile, %				
0-25	23.6% (n = 21,309)	30.3% (n = 32,058)	27.7% (n = 3089)	27.2% (n = 56,455)
26-50	25.3% (n = 22,837)	26.1% (n = 27,621)	25.7% (n = 2852)	25.7% (n = 53,309)
51-75	24.0% (n = 21,667)	22.0% (n = 23,225)	22.9% (n = 2552)	22.9% (n = 47,445)
76-100	27.1% (n = 24,441)	21.6% (n = 22,882)	24.0% (n = 2676)	24.1% (n = 50,000)
Hospital characteristics				
Teaching facility	54.2% (n = 49,824)	52.6% (n = 56,603)	55.6% (n = 6321)	53.5% (n = 112,749)
Hospital region				
Northeast	27.5% (n = 25,301)	21.6% (n = 23,306)	26.7% (n = 3034)	24.4% (n = 51,642)
Midwest	22.7% (n = 20,931)	25.4% (n = 27,443)	21.4% (n = 2435)	24.0% (n = 50,808)
South	33.2% (n = 30,540)	37.3% (n = 40,363)	36.3% (n = 4127)	35.5% (n = 75,030)
West	16.6% (n = 15,257)	15.7% (n = 17,013)	15.7% (n = 1784)	16.1% (n = 34,054)
Bed size				
Small	8.6% (n = 7940)	9.2% (n = 9918)	8.6% (n = 980)	8.9% (n = 18,837)
Medium	22.7% (n = 20,823)	21.7% (n = 23,328)	21.2% (n = 2414)	22.1% (n = 46,564)
Large	68.7% (n = 63,116)	69.1% (n = 74,363)	70.1% (n = 7968)	69.0% (n = 145,447)
Urban location	93.5% (n = 85,888)	93.2% (n =100,326)	92.2% (n = 10,472)	93.3% (n = 196,687)
Inpatient case characteristics				
LOS	12.0 (±10.5)	9.4 (±10.1)	14.7 (±11.6)	10.9 (±11.5)
No. of diagnoses	10.8 (±4.3)	12.0 (±4.9)	12.0 (±4.6)	11.5 (±4.7)
No. of procedures	4.1 (±2.6)	5.8 (±2.7)	7.3 (±3.1)	5.1 (±2.9)
Deyo-Charlson Comorbidity Index	2.2 (±1.3)	2.5 (±1.5)	2.3 (±1.3)	2.4 (±1.4)
Year				
2001	12.5% (n = 11,483)	4.2% (n = 4583)	7.2% (n = 816)	8.0% (n = 16,882)
2002	12.6% (n = 11,608)	4.2% (n = 4573)	9.3% (n = 1057)	8.1% (n = 17,238)
2003	12.2% (n = 11,183)	5.8% (n = 6313)	10.1% (n = 1149)	8.8% (n = 18,645)
2004	11.2% (n = 10,344)	7.2% (n = 7793)	10.0% (n = 1134)	9.1% (n = 19,271)
2005	9.8% (n = 9064)	8.5% (n = 9243)	10.2% (n = 1155)	9.2% (n = 19,462)
2006	9.0% (n = 8268)	12.9% (n = 13,979)	11.2% (n = 1279)	11.1% (n = 23,467)
2007	8.7% (n = 8018)	14.4% (n = 15,534)	11.0% (n = 1252)	11.7% (n = 24,804)
2008	8.4% (n = 7717)	14.4% (n = 15,538)	11.4% (n = 1296)	11.6% (n = 24,549)
2009	8.1% (n = 7450)	14.5% (n = 15,705)	9.9% (n = 1130)	11.5% (n = 24,285)
2010	7.5% (n = 6893)	13.8% (n = 14,926)	9.8% (n = 1112)	10.8% (n = 22,931)

LOS, Length of stay.

design.[11] Analyses were performed using SAS version 9.2 (Cary, NC) and Stata SE version 12.1 (College Station, Tex).

RESULTS

Descriptive statistics. A total of 2,497,363 inpatient DFU cases were observed from 2001 to 2010 across 388.4 million total inpatient admissions, with 16.5% (n = 412,051) involving amputations (major = 34.8%, minor = 65.2%) and 8.5% (n = 211,534) involving a revascularization procedure (open only = 43.5%, EVT only = 51.1%, combination = 5.4%). Of the 143,470 major amputations, 6.7% (n = 9600) involved revascularization during the same hospital stay (open only = 29.8%, EVT only = 63.5%, combination = 6.7%) vs 15.1% (n = 40,422) of the 268,520 minor amputations (open only = 44.9%, EVT only = 44.2%, combination = 6.9%). Overall, the major:minor amputation ratio was 0.534, and those involving any revascularization equaled 0.237.

In a comparison of 2001 with 2010 (Fig), the volume of overall DFU cases involving any open procedure decreased 34.9% (from 12,300 to 8005), and EVT volume increased 197.1% (from 5399 to 16,038). Within this population, minor amputations increased 48.5% (from 21,545 to 32,000), and major amputations increased 7.7% (from 13,067 to 14,069 cases). Among amputation-only cases, in a comparison of 2001 vs 2010, open volume decreased 27.3% (from 2878 to 2091) and EVT increased 180.3% (from 1077 to 4096), and was relatively flat as a percentage of DFU cases (Fig). Importantly, an increasing case-mix severity was seen for amputations with associated vascular procedures from 2001 to 2010; the Deyo-Charlson Comorbidity Index increased slightly but significantly for major amputations (from 2.25 to 3.04; $P < .001$) and for

Table II. Descriptive statistics, stratified according to single procedure and amputation type

Variable	*Open bypass procedure only, major amputation (n = 2865)*	*Open bypass procedure only, minor amputation (n = 19,750)*	*Open bypass procedure only, no amputation (n = 69,414)*
Patient characteristics			
Age	67.0 (±10.9)	67.5 (±11.2)	69.0 (±11.2)
Charges (U.S., 2012)	$194,413 (±170,938)	$118,568 (±10,591)	$78,253 (±74,967)
Total national bill (U.S., 2012)	$0.55 billion	$2.29 billion	$5.31 billion
Female sex	39.9% (n = 1144)	33.7% (n = 6663)	41.2% (n = 28,617)
Income quartile, %			
0-25	28.8% (n = 807)	24.7% (n = 4781)	23.1% (n = 15,721)
26-50	23.9% (n = 670)	24.3% (n = 4708)	25.6% (n = 17,459)
51-75	23.6% (n = 660)	24.6% (n = 4768)	23.8% (n = 16,239)
76-100	23.8% (n = 667)	26.3% (n = 5088)	27.4% (n = 18,687)
Hospital characteristics			
Teaching facility	58.3% (n = 1667)	54.7% (n = 10795)	53.9% (n = 37362)
Hospital region			
Northeast	29.1% (n = 834)	30.3% (n = 5985)	26.6% (n = 18,482)
Midwest	19.1% (n = 546)	20.7% (n = 4086)	23.5% (n = 16,298)
South	36.2% (n = 1038)	33.6% (n = 6640)	32.9% (n = 22,863)
West	15.6% (n = 447)	15.4% (n = 3039)	17.0% (n = 11,771)
Bed size			
Small	6.4% (n = 184)	8.4% (n = 1658)	8.8% (n = 6098)
Medium	23.8% (n = 680)	23.0% (n = 4544)	22.5% (n = 15,599)
Large	69.8% (n = 1997)	68.6% (n = 13,521)	68.7% (n = 47,598)
Urban location	94.7% (n = 2710)	93.9% (n = 18,512)	93.3% (n = 64,667)
Inpatient case characteristics			
LOS	27.2 (±10.9)	16.7 (±10.9)	10.1 (±8.6)
No. of diagnoses	12.7 (±4.9)	11.6 (±4.4)	10.5 (±4.1)
No. of procedures	6.7 (±3.2)	5.6 (±2.6)	3.6 (±2.4)
Deyo-Charlson Comorbidity Index	2.5 (±1.3)	2.4 (±1.3)	2.2 (±1.3)
Year			
2001	11.5% (n = 331)	11.7% (n = 2316)	12.7% (n = 8837)
2002	13.0% (n = 372)	13.2% (n = 2611)	12.4% (n = 8624)
2003	9.8% (n = 181)	12.9% (n = 2555)	12.0% (n = 8346)
2004	12.9% (n = 371)	11.5% (n = 2272)	11.1% (n = 7702)
2005	10.2% (n = 293)	9.8% (n = 1941)	9.8% (n = 6829)
2006	11.7% (n = 336)	8.5% (n = 1671)	9.0% (n = 6261)
2007	8.2% (n = 236)	9.0% (n = 1778)	8.6% (n = 6004)
2008	7.9% (n = 227)	8.0% (n = 1583)	8.5% (n = 5907)
2009	7.0% (n = 200)	7.5% (n = 1488)	8.3% (n = 5763)
2010	7.6% (n = 217)	7.8% (n = 1535)	7.4% (n = 5141)

LOS, Length of stay.

minor amputations (from 2.14 to 2.75; $P < .001$). Unadjusted mean charges per admission also increased by 25.5% (from $104,839 to $131,554, $P < .001$) and the mean LOS decreased by 22.5% (from 18.4 to 14.2; $P < .001$). Inpatient amputation-related mortality was generally low across all DFU cases, involving amputation at 1.7% and decreased in total cases by 19.1% (from 749 [4.4%] to 606 [2.6%]; $P < .001$). The mortality rate for major amputation was 6.3% (open = 6.3%, EVT = 6.3%; $P = .963$ [not significant]) vs 1.3% for minor amputation (open = 1.4%, EVT = 1.2%; $P = .162$ [not significant]). The overall presence of any key surgical complications summed to 10.1%, increasing slightly from 10.2% to 10.8% by 2010, representing a small, yet statistically significant, proportional change ($P < .023$). In Tables I to IV, descriptive statistics for DFU cases with revascularization according to procedure alone (Tables I and III) and additionally according to amputation type (Tables II and IV) are shown; in Fig, revascularization procedure volume and percentage involving amputation across the study's time frame are shown.

Multivariate analysis. Based on an initial assessment of crude, unadjusted, descriptive statistics in an assessment of open vs EVT across the 2001 to 2010 time horizon, open procedures generally appeared to have a higher rate of overall surgical complications, similar to slightly greater inpatient mortality, charges, and a longer LOS. In controlling for other factors (ie, patient demographic and hospital characteristics, case-mix severity), results are shown for the adjusted multivariate analyses of procedure type according to amputation status for clinical (Table V) and economic outcomes (Table VI).

Concerning adjusted analyses of clinical outcomes from 2001 to 2010 (Table V), significant increases (ie, P value less than the Simes false discovery rate of $P < .023$) in the presence of any surgical complication from 2001 exceeding 50% were noted for open procedures involving

Table II. Continued.

Endovascular procedure only, major amputation (n = 6096)	*Endovascular procedure only, minor amputation (n = 17,882)*	*Endovascular procedure only, no amputation (n = 84,147)*
67.0 (±10.9)	66.8 (±12.0)	69.2 (±11.8)
\$165,225 (±132,324)	\$111,015 (±86,350)	\$77,523 (±70,531)
\$0.99 billion	\$1.95 billion	\$6.44 billion
40.5% (n = 2471)	35.0% (n = 6265)	44.7% (n = 37,647)
32.3% (n = 1922)	30.2% (n = 5260)	30.2% (n = 24,877)
27.7% (n = 1648)	25.4% (n = 4423)	26.1% (n = 21,550)
21.8% (n = 1296)	21.9% (n = 3813)	22.0% (n = 18,116)
18.2% (n = 1079)	22.5% (n = 3928)	21.7% (n = 17,875)
55.7% (n = 3380)	53.8% (n = 9571)	52.1% (n = 43652)
18.0% (n = 1096)	22.3% (n = 3990)	21.7% (n = 18,220)
22.1% (n = 1347)	23.8% (n = 4257)	26.0% (n = 21,839)
41.9% (n = 2557)	39.1% (n = 6988)	36.6% (n = 30,817)
18.0% (n = 1096)	14.8% (n = 2647)	15.8% (n = 13,271)
8.6% (n = 524)	8.8% (n = 1563)	9.3% (n = 7831)
23.4% (n = 1422)	21.4% (n = 3798)	21.6% (n = 18,107)
67.9% (n = 4121)	69.9% (n = 12,427)	69.0% (n = 57,815)
92.7% (n = 5622)	93.3% (n = 16,690)	93.1% (n = 78,014)
21.1 (±15.1)	13.7 (±9.5)	7.7 (±8.9)
14.2 (±5.5)	13.2 (±5.0)	11.53 (±4.7)
7.8 (±3.3)	6.9 (±2.7)	5.4 (±2.5)
2.9 (±1.5)	2.6 (±1.5)	2.5 (±1.5)
3.8% (n = 234)	3.4% (n = 612)	4.4% (n = 3736)
4.7% (n = 287)	3.6% (n = 638)	4.3% (n = 3648)
7.9% (n = 481)	5.4% (n = 957)	5.8% (n = 4875)
6.2% (n = 378)	6.7% (n = 1195)	7.4% (n = 6220)
9.1% (n = 553)	8.5% (n = 1513)	8.5% (n = 7176)
13.5% (n = 822)	12.1% (n = 2165)	13.0% (n = 10,933)
15.4% (n = 938)	13.8% (n = 2463)	14.4% (n = 12,133)
11.2% (n = 680)	14.2% (n = 2543)	14.6% (n = 12,313)
14.6% (n = 889)	16.1% (n = 2872)	14.2% (n = 11,943)
13.7% (n = 833)	16.3% (n = 2923)	13.3% (n = 11,169)

minor amputations (OR_{2008} = 1.66, OR_{2009} = 1.77, OR_{2010} = 1.74) and exceeding 30% for open procedures involving no amputations (OR_{2008} = 1.64, OR_{2009} = 1.37, OR_{2010} = 1.53). A marked and significant increase in any surgical complication was observed for EVT use in major amputations beginning in 2007 (OR_{2007} = 11.27, OR_{2009} = 11.36, OR_{2010} = 11.80).

Consistent with the aforementioned findings, the total number of surgical complications (Table V) was significantly greater (ie, *P* value less than the Simes false discovery rate of $P < .023$) for open procedures involving minor amputations exceeding 50% beginning in 2008 (IRR_{2008} = 1.52, IRR_{2009} = 1.56, IRR_{2010} = 1.74) and more than 33% for open procedures involving no amputation beginning in 2008 (IRR_{2008} = 1.53, IRR_{2009} = 1.33, IRR_{2010} = 1.43). Large, statistically significant increases in the total number of surgical complications exceeding approximately ≥900% were observed for EVT involving major amputations for several years vs 2001 (IRR_{2007} = 9.99, IRR_{2009} = 10.64, IRR_{2010} = 10.70).

The multivariate analyses of inpatient mortality (Table V) suggested a significantly lower (ie, *P* value less than the Simes false discovery rate of $P < .023$) odds of almost ≥50% for open procedures with no amputations in 2009 (OR_{2009} = 0.30). Decreased odds of inpatient mortality of approximately ≤50% were observed for several years involving EVT without amputations (OR_{2004} = 0.47, OR_{2007} = 0.37, OR_{2008} = 0.29, OR_{2009} = 0.37, OR_{2010} = 0.36).

Significantly increased charges (ie, *P* value less than the Simes false discovery rate of $P < .023$) were observed over time for most procedures and amputation status (Table VI), with the exception of no significant change noted with open procedure with major amputation. Hospital LOS decreased by approximately 10% to 25% across most of the groups by 2009 or 2010.

DISCUSSION

This investigation of revascularization procedures in DFU cases provides nationally-representative clinical and

Table III. Descriptive statistics of clinical outcomes, stratified according to procedure

	Open bypass procedure only (n = 92,029)		*Endovascular procedure only (n = 108,124)*		*Open bypass with endovascular procedure, combined (n = 11,381)*		*Overall, any revascularization (N = 211,534)*	
Outcome assessments	*Percentage*	*No.*	*Percentage*	*No.*	*Percentage*	*No.*	*Percentage*	*No.*
Amputation	24.6	22,615	22.2	23,988	30.1	3429	23.7	50,032
Major	3.1	2865	5.6	6096	5.6	638	4.5	9600
Minor	21.5	19,750	16.5	17,882	24.5	2791	19.1	40,422
Any surgical complication	14.4	13,267	5.8	6300	16.6	1889	10.1	21,455
Cardiac	2.4	2222	0.7	723	2.4	279	1.5	3224
Stroke	0.2	139	0.1	45	0.4	45	0.1	228
Respiratory	2.0	1877	0.6	654	2.7	303	1.3	2834
Bleeding	8.7	7968	3.1	3350	9.6	1090	5.9	12,408
Infection	2.5	2344	1.8	1911	3.1	349	2.2	4604
Shock	0.1	117	0.1	72	0.2	21	0.1	209
Died during hospitalization	1.7	1516	1.6	1778	2.5	288	1.7	3582

Table IV. Descriptive statistics of clinical outcomes, stratified according to single procedure and amputation

	Open bypass procedure only, major amputation (n = 2865)		*Open bypass procedure only, minor amputation (n = 19,750)*		*Open bypass procedure only, no amputation (n = 69,414)*		*Endovascular procedure only, major amputation (n = 6096)*		*Endovascular procedure only, minor amputation (n = 17,882)*		*Endovascular procedure only, no amputation (n = 84,147)*	
Outcome assessments	*Percentage*	*No.*	*Percentage*	*No.*	*Percentage*	*No.*	*Percentage*	*No.*	*Percentage*	*No.*	*Percentage*	*No.*
Any surgical complication	22.8	654	14.4	2846	14.1	9767	15.5	5152	7.3	1312	4.8	4043
Cardiac	2.9	84	2.2	427	2.5	1711	1.4	86	0.8	148	0.6	490
Stroke	0.4	11	0.1	29	0.1	99	0.1	5	0.0	0	0.1	39
Respiratory	4.2	122	1.7	327	2.1	1428	2.1	129	0.7	127	0.5	397
Bleeding	12.0	345	9.0	1773	8.4	5850	9.9	604	4.3	774	2.3	1973
Infection	8.0	228	2.5	494	2.3	1622	3.5	210	1.8	329	1.6	1372
Shock	0.7	20	0.2	30	0.1	67	0.1	5	0.1	10	0.1	57
Died during hospitalization	6.3	179	1.4	278	1.5	1059	6.3	384	1.2	222	1.4	1172

economic characteristics within U.S. inpatient settings from 2001 to 2010. Overall, 16.5% of the 2.5 million total DFU cases involved an amputation (n = 412,057), of which almost half underwent any revascularization procedure (n = 211,534). The total national bill summed to $18.99 billion (USD 2012) with a case mortality rate of 9.3% and a surgical case complication rate of 10.1%. Concerning single-procedure cases only, the highest charges involved open procedures with major amputations at $194,413 (USD 2012), also incurring the highest surgical complication rate of 22.8% and longest LOS of 27.2 days. Open procedure volume declined sharply during the study's time frame and was paralleled by marked increases in EVT volume, confirming reports that have observed a paradigm shift in the management of lower extremity peripheral artery disease, even for limb salvage cases.[6-10] We also found improvements concerning short-term inpatient mortality, with a significant reduction of 19.1% in the crude case rate from 2001 to 2010. After adjusting for key covariates (ie, sociodemographic attributes, hospital characteristics, comorbid conditions), significant and consistent reductions in inpatient death were observed among cases particularly involving EVT without amputations (ie, 2006-2010 vs 2001). Results of the stratified multivariate analyses of surgical complications suggested instances in which outcomes worsened over time, as large and significantly greater odds of surgical complications among EVT with major amputations began in 2007 (vs 2001), reaching a maximum of 1008.2% in 2010. An increased rate of complications was also noted among open procedures with either minor or no amputations. Regarding economic outcomes, hospital LOS was observed to decrease for most procedures and amputation types, and inflation-adjusted charges generally increased.

To place the current study in perspective, Goodney et al reported that for every single lower extremity bypass performed, three EVT interventions were conducted in an examination of Medicare part B claims from 1996 to 2006; EVT also increased 229.8% (from 138 to 455 procedures per 100,000 beneficiaries) and open bypass decreased 42% (from 219 to 126 per 100,000 beneficiaries).[6] Egorova et al noted a 209% increase in EVT

Table V. Multivariate regression analyses of clinical outcomes, stratified according to single procedure and amputation

Year	*Open bypass procedure only, major amputation (n = 2865)*		*Open bypass procedure only, minor amputation (n = 19,750)*		*Open bypass procedure only, no amputation (n = 69,414)*		*Endovascular procedure only, major amputation (n = 6096)*		*Endovascular procedure only, minor amputation (n = 17,882)*		*Endovascular procedure only, no amputation (n = 84,147)*	
Any surgical complication[a]	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*
2001 (baseline)												
2002	0.63	0.23-1.69	0.94	0.56-1.57	1.07	0.84-1.36	3.54	0.37-33.50	3.20	0.98-10.42	0.76	0.43-1.34
2003	1.78	0.71-4.45	1.13	0.77-1.66	0.92	0.73-1.16	6.19	0.77-49.76	2.71	0.84-8.75	1.04	0.64-1.68
2004	1.67	0.69-4.05	1.53	1.04-2.25	1.19	0.94-1.51	7.18	0.90-57.34	2.21	0.71-6.89	0.98	0.62-1.56
2005	1.81	0.67-4.85	1.20	0.76-1.89	1.08	0.83-1.41	7.71	0.95-62.50	2.12	0.69-6.49	1.15	0.74-1.78
2006	1.30	0.52-3.22	1.25	0.83-1.89	1.08	0.85-1.37	5.84	0.74-45.98	2.28	0.77-6.76	0.81	0.52-1.26
2007	1.35	0.45-4.02	1.29	0.81-2.04	1.25	0.99-1.58	11.27[b]	1.48-85.70	2.64	0.90-7.76	0.81	0.53-1.25
2008	2.26	0.83-6.12	1.66	1.11-2.48	1.64[b]	1.27-2.13	8.36	1.10-63.79	2.76	0.95-8.04	0.96	0.63-1.45
2009	2.15	0.77-6.02	1.77[b]	1.15-2.72	1.37[b]	1.07-1.75	11.36[b]	1.45-89.10	2.95	1.00-8.69	1.09	0.71-1.68
2010	2.73	0.92-8.17	1.74[b]	1.11-2.73	1.53[b]	1.18-2.00	11.80[b]	1.55-90.16	2.73	0.93-7.96	1.04	0.67-1.59
Surgical complication, No. (sum)[c]	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*
2001 (baseline)												
2002	0.75	0.30-1.85	0.92	0.58-1.44	1.10	0.87-1.37	3.33	0.38-29.16	3.00	0.98-9.19	0.81	0.47-1.39
2003	1.96	0.90-4.30	1.08	0.76-1.53	0.95	0.77-1.17	6.15	0.81-46.45	2.90	0.94-8.97	1.04	0.66-1.66
2004	1.30	0.62-2.73	1.34	0.98-1.95	1.20	0.97-1.48	7.68	1.02-57.89	2.14	0.72-6.37	1.02	0.64-1.60
2005	1.40	0.64-3.07	1.20	0.80-1.80	1.08	0.85-1.37	7.33	0.97-55.44	2.16	0.73-6.38	1.20	0.78-1.84
2006	1.01	0.47-2.15	1.18	0.82-1.69	1.08	0.87-1.34	6.05	0.82-44.81	2.25	0.79-6.38	0.81	0.53-1.23
2007	1.39	0.57-3.40	1.25	0.82-1.89	1.26[b]	1.01-1.56	9.99[b]	1.39-71.85	2.50	0.89-7.03	0.85	0.56-1.29
2008	1.68	0.74-3.82	1.52[b]	1.06-2.16	1.53[b]	1.23-1.89	9.06[b]	1.25-65.72	2.88	1.03-8.05	0.99	0.66-1.49
2009	1.35	0.60-3.03	1.56[b]	1.08-2.27	1.33[b]	1.07-1.66	10.64[b]	1.45-78.34	2.97	1.05-8.39	1.07	0.71-1.62
2010	1.77	0.78-4.00	1.74[b]	1.19-2.56	1.43[b]	1.14-1.79	10.70[b]	1.48-77.23	2.78	0.99-7.79	1.03	0.68-1.55
Inpatient death[a]	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*
2001 (baseline)												
2002	2.73	0.55-13.67	1.06	0.39-2.93	0.70	0.41-1.18	1.04	0.24-4.43	0.29	0.03-2.77	0.61	0.29-1.29
2003	5.60	0.98-31.94	0.91	0.29-2.80	0.58	0.32-1.05	0.90	0.25-3.32	0.32	0.05-2.13	0.92	0.47-1.81
2004	3.04	0.61-15.06	0.89	0.24-3.33	0.76	0.44-1.34	0.51	0.11-2.38	1.06	0.23-4.83	0.47	0.23-0.99
2005	5.44	1.02-28.95	1.09	0.35-3.43	0.79	0.45-1.41	0.77	0.21-2.88	0.46	0.10-2.11	0.67	0.35-1.28
2006	0.86	0.07-9.93	1.23	0.39-3.87	0.73	0.41-1.31	0.86	0.25-2.98	0.45	0.10-1.92	0.61	0.34-1.11
2007	1.16	0.19-12.33	0.55	0.16-2.12	0.50	0.26-0.96	0.58	0.16-2.08	0.37	0.09-1.48	0.37[b]	0.19-0.69
2008	1.70	0.19-15.25	0.93	0.29-3.00	0.63	0.34-1.17	0.22	0.05-0.96	0.40	0.09-1.66	0.29[b]	0.15-0.58
2009	1.12	0.09-14.70	0.37	0.08-1.73	0.30[b]	0.13-0.69	0.26	0.06-1.11	0.17	0.03-0.89	0.37[b]	0.19-0.69
2010	0.85	0.07-10.61	0.58	0.16-2.13	0.55	0.28-1.09	0.61	0.17-2.23	0.17	0.03-0.93	0.36[b]	0.19-0.67

CI, Confidence interval; *IRR,* incidence rate ratio; *OR,* odds ratio.
Multivariate models were adjusted for: patient demographic characteristics (age, sex, income level), hospital characteristics (bed size, geographic region, urban/rural location, teaching status), and Deyo-Charlson Comorbidity Index (case-mix comorbid risk adjustor/disease complexity).
[a]Generalized linear model, binomial/logistic.
[b]Statistical significance less than the computed Simes false discovery rate *P* value ($P < .023$).
[c]Generalized linear model, Poisson.

(from 45 to 94 per 100,000 population) and a decrease of 39% in open revascularizations (from 111 to 68 per 100,000 population) among inpatient cases from 1998 to 2007.[7] Concerning critical limb ischemia cases in North Carolina in 1996 and 2005, Cull et al found a 255% increase for EVT (from 151 to 385 total cases) and an 11% decrease for open procedures (from 420 to 373 total cases).[9] Comparatively, in the current study we found an increase in EVT of 126.3% (from 2570 to 5815 per 100,000 DFU cases) and a decrease in open bypass of 49.6% (from 5855 to 2902 per 100,000 DFU cases).

Relating to amputations, from 1996 vs 2006, Goodney et al reported a 28.5% decrease (from 263 to 188 per 100,000 beneficiaries), and Egorova et al found a decrease of 38% (from 59 to 37 per 100,000 population) from 1998 vs 2007.[6,7] Although most cases in Egorova et al involved critical limb ischemia and peripheral artery disease, diabetes was present in 60% of critical limb ischemia cases and 30% of claudication cases.[7] In the present study, the overall crude amputation case rate was markedly higher, and did not appreciably change between 2001 and 2010 (from 16,476 to 16,702 per 100,000 DFU cases); minor amputations

Table VI. Multivariate regression analyses of economic outcomes, stratified according to procedure and amputation

Year	*Open bypass procedure only, major amputation (n = 2865)*		*Open bypass procedure only, minor amputation (n = 19,750)*		*Open bypass procedure only, no amputation (n = 69,414)*		*Endovascular procedure only, major amputation (n = 6096)*		*Endovascular procedure only, minor amputation (n = 17,882)*		*Endovascular procedure only, no amputation (n = 84,147)*	
Charges[a]	*exp(b)*	*95% CI*	*exp(b)*	*95% CI*	*exp(b)*	*95% CI*	*exp(b)*	*95% CI*	*exp(b)*	*95% CI*	*exp(b)*	*95% CI*
2001 (baseline)												
2002	1.09	0.81-1.47	1.14	0.95-1.36	1.09	0.98-1.21	1.17	0.85-1.62	1.10	0.92-1.31	1.11	0.99-1.23
2003	1.34	1.01-1.77	1.19[b]	1.04-1.35	1.19[b]	1.08-1.30	1.24	0.96-1.60	1.43[b]	1.17-1.75	1.29[b]	1.16-1.44
2004	1.27	0.97-1.66	1.17[b]	1.04-1.32	1.21[b]	1.09-1.34	1.27	0.95-1.68	1.33[b]	1.16-1.53	1.34[b]	1.20-1.50
2005	1.17	0.87-1.58	1.18[b]	1.03-1.36	1.18[b]	1.06-1.30	1.27	0.99-1.62	1.45[b]	1.24-1.70	1.47[b]	1.30-1.66
2006	1.12	0.87-1.45	1.25[b]	1.09-1.44	1.22[b]	1.10-1.36	1.43[b]	1.13-1.80	1.38[b]	1.20-1.57	1.38[b]	1.24-1.52
2007	1.18	0.91-1.53	1.24[b]	1.09-1.42	1.17[b]	1.06-1.28	1.39[b]	1.08-1.78	1.39[b]	1.22-1.58	1.40[b]	1.25-1.56
2008	1.18	0.90-1.55	1.24[b]	1.08-1.42	1.18[b]	1.07-1.31	1.37[b]	1.09-1.72	1.45[b]	1.26-1.67	1.49[b]	1.33-1.67
2009	1.13	0.81-1.58	1.29[b]	1.11-1.50	1.21[b]	1.08-1.35	1.36[b]	1.09-1.69	1.38[b]	1.21-1.58	1.55[b]	1.39-1.72
2010	1.23	0.92-1.65	1.36[b]	1.16-1.58	1.33[b]	1.19-1.49	1.38[b]	1.10-1.73	1.40[b]	1.23-1.60	1.64[b]	1.47-1.83
LOS[c]	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*	*IRR*	*95% CI*
2001 (baseline)												
2002	0.93	0.76-1.13	1.00	0.92-1.09	0.99	0.92-1.07	0.95	0.74-1.22	1.05	0.90-1.23	1.08	0.94-1.24
2003	0.96	0.78-1.17	1.00	0.91-1.10	0.98	0.91-1.04	0.95	0.74-1.21	1.12	0.95-1.29	1.08	0.95-1.23
2004	1.06	0.85-1.33	0.98	0.90-1.07	0.99	0.92-1.07	0.93	0.72-1.19	1.05	0.92-1.21	1.05	0.92-1.18
2005	0.94	0.75-1.16	0.98	0.89-1.08	0.93	0.87-1.00	0.92	0.73-1.17	1.07	0.94-1.22	1.05	0.94-1.18
2006	0.91	0.76-1.09	1.00	0.91-1.10	0.89[b]	0.82-0.95	0.99	0.79-1.24	1.01	0.89-1.15	0.94	0.83-1.08
2007	0.89	0.72-1.09	0.96	0.87-1.05	0.82[b]	0.76-0.88	0.94	0.73-1.21	0.99	0.87-1.12	0.88	0.77-0.99
2008	0.93	0.74-1.17	0.91	0.83-1.00	0.81[b]	0.75-0.88	0.87	0.70-1.09	0.95	0.82-1.08	0.92	0.80-1.05
2009	0.71[b]	0.54-0.95	0.85[b]	0.77-0.94	0.76[b]	0.70-0.82	0.78	0.63-0.97	0.91	0.81-1.03	0.92	0.81-1.04
2010	0.75[b]	0.60-0.94	0.88[b]	0.80-0.97	0.82[b]	0.76-0.89	0.76[b]	0.61-0.96	0.85[b]	0.75-0.95	0.91	0.81-1.03

CI, Confidence interval; *exp(b),* exponentiated beta coefficient; *IRR,* incidence rate ratio, *LOS,* length of stay.

Multivariate models were adjusted for: patient demographic characteristics (age, sex, income level), hospital characteristics (bed size, geographic region, urban/rural location, teaching status), and Deyo-Charlson Comorbidity Index (case-mix comorbid risk adjustor/disease complexity).

[a]Generalized linear model, gamma.

[b]Statistical significance less than the computed Simes false discovery rate *P* value ($P < .023$).

[c]Generalized linear model, negative binomial.

averaged 10.8% of cases and major amputations averaged 5.7%. In observing decreased number of amputations with increased EVT, Goodney et al suggested that improvements of care might have occurred, noting that a more critical evaluation of comorbidities and podiatric care was still required.[6,17,18] These authors suggested that improved access to podiatric care, more frequent testing for hemoglobin A1c, and hyperlipidemia treatment might have also contributed to improved outcomes.[6] Despite this, and more consistent with the current study's results, Anderson et al found 10-fold increases in endovascular procedures with no notable change in amputations across inpatient hospitalizations in the United States from 1980 to 2000.[10] Cull et al also reported no significant changes in amputation rates between 1995 and 2006 among critical limb ischemia revascularization cases in South Carolina.[9] Although Goodney et al commented that the period of decline for amputations followed the time horizon analyzed by Anderson et al, findings from the current work did not suggest a significant proportional change in overall amputation rate among DFU cases.[6,10] The large increase in EVT that occurred without a change in amputation rates might suggest that either EVT was required to yield similar results as open, or that a larger number of procedures were performed than were required for actual limb salvage.

Concerning surgical complications, Egorova et al reported no changes among major amputations with revascularization in 1998 vs 2007 involving crude rates of cardiac complications, postoperative stroke, respiratory complications, or infection; bleeding, however, was found to decrease significantly (from 23.1% to 16.7%; $P = .0004$).[7] Diabetes, in particular, was found to be associated with >60% of major amputations, although the number of revascularization-associated complications in this high-risk cohort was found to decrease over time.[7] Comparatively, changes in the crude rates among specific categories of complications in 2001 vs 2010 among major amputation with revascularizations across all DFU cases were unchanged for cardiac, stroke, respiratory, and infection. Bleeding, however, was found to significantly increase from 5.00% to 17.53% ($P < .001$), comprised of bleeding in EVT (from <0.01% to 14.77%; $P < .001$) vs open (from 9.37% to 26.27%; $P < .001$). Results of the current study's stratified multivariate analyses did not uniformly support the conclusion of Egorova et al, because the presence of any surgical complication was noted to increase significantly for endovascular procedures with major amputations.[7] To a lesser extent, complications increased among open procedures with either minor amputations or without amputation. Across many subsets, complications between open and EVT remained similar, which might suggest that less-invasive approaches might not translate to decreased risk overall, particularly if repeated procedures are ultimately required. Regardless, evidence suggests improvement in clinical outcomes with repeated target extremity revascularization among patients with diabetes and those without, and that current standards of care yield similar outcomes in terms of limb salvage, survival, and major amputations.[19,20] In this context, Cull et al reported a significant increase from 8% to 19% of critical limb ischemia cases in North Carolina requiring additional revascularization in the same calendar year in 1996 and 2005, respectively ($P < .001$).[9]

Collectively, the large economic effect of amputations despite EVT or bypass implies the need to develop and validate risk stratification for patients who might or might not benefit from costly and potentially risky procedures. In the current work, costs from the perspective of the payer were generally found to increase from 2001 across almost all procedures and amputation categories, with the largest significant increases in 2010 vs 2001 observed among endovascular procedures (major amputation = 37.9%, minor amputation = 40.1%, no amputation = 64.0%). Similarly, in 2010, LOS was found to either decrease or remain constant vs 2001, particularly among open procedures (major amputation = 25.0%, minor amputation = 12.0%, no amputation = 18.2%). Across all DFU cases in the United States from 2001 to 2010, irrespective of revascularization procedures, Skrepnek et al reported increased charges of 16.7% and a decreased LOS of 23.6%.[21] Nguyen et al analyzed resource utilization within the Project of Ex-Vivo vein graft Engineering via Transfection III (PREVENT III) clinical trial of critical limb ischemia patients who received lower extremity bypass, and reported an initial, index LOS of 8.8 days and cumulative LOS of 24.8 days after an average of 1.5 hospitalizations across the 1-year study period.[22] Factors including advanced age, complications, and illness severity were among those found to be strongly associated with inpatient mortality or resource utilization by Kazmers et al.[23] Although we did not explicitly report results of socioeconomic factors (eg, income, geographic location, hospital characteristics), control for these key attributes was indeed undertaken within the multivariate analysis; inclusion of these variables is required based on economic theory and previous clinical work.[7,8,24-29] To illustrate, Durham et al assessed the association between socioeconomic status, clinical outcomes, and inpatient hospital costs among 187 regional cases of femoropopliteal revascularization from 2003 to 2006, suggesting that lower income levels were associated with higher per-day cost of patency and inferior limb salvage.[24] Furthermore, comorbidities including coronary artery disease, heart failure, diabetes, and hypertension were also not found to be associated with the study's outcomes. Goodney et al also assessed geographic differences in vascular care procedures and amputation rates among Medicare beneficiaries from 2003 to 2006, and suggested that regions of high-intensity vascular care (ie, lower extremity vascular procedures) were associated with decreased likelihoods of amputations without preliminary attempts at revascularization.[29]

Although in the current investigation we used nationally-representative data for revascularizations among DFU cases, potential limitations should be addressed. Despite analyses that controlled for key factors known to be associated with outcomes and because these data were not explicitly administrative claims, other unmeasurable or exogenous factors might be of importance in interpreting findings including reimbursement coding changes and the dataset's lack of ability to stratify according to indication, extent of wound, degree of ischemia, and severity of infection.[30] Although a validated case-mix comorbidity index and method to identify DFUs was used, specific clinical criteria to establish detailed revascularization types, specific ischemic ulcers, or infection severity beyond broad diagnostic criteria was not present, nor was information relating to ambulatory care.[12,13] The unit of analysis was also that of a specific inpatient admission rather than of a specific patient, hence, the methodological framework could not explicitly identify multiple visits by the same person. Because explicit longitudinal analysis of the individuals could not be undertaken, certain findings (eg, case mortality) might be markedly underestimated because of hospital readmissions. Furthermore, the broad inclusion criteria to identify DFU cases did not necessarily preclude these as being the principal reason or diagnosis associated with the inpatient admission.[12] Generalizing findings from this work to specific, individual hospital systems or patients should therefore be undertaken with caution. Despite these potential limitations, the current study builds on previous research through its explicit empirical control for key factors related to outcomes rather than only crude, unadjusted findings. Future avenues of research in assessing cost, outcomes, and access to care in patients with DFUs might seek to include comprehensive analyses across all health care settings in addition to disease-specific clinical factors that can ultimately establish the appropriateness of various revascularization procedures.

CONCLUSIONS

In this nationally-representative investigation, we found that admissions involving DFUs are common, long, and costly (often >$100,000 per case), potentially due in part to the increasing case-severity mix seen within inpatient settings. More DFU cases involved revascularization (8.5% per admission), with a large shift from open bypass to EVT. It is encouraging to note that hospital mortality and LOS either remained the same or have decreased significantly, and that major amputations for hospitalized patients with DFU also appear to be flattening with an increase in minor amputations (major:minor ratio = 0.534). The news is mixed, however, because increases in procedure-specific surgical complications and increased inflation-adjusted charges were observed across several intervention categories. Collectively, these findings characterize the prevalence, clinical significance, and economic effect of a frequently neglected problem: the DFU.

AUTHOR CONTRIBUTIONS

Conception and design: GS, DA, JM
Analysis and interpretation: GS, DA, JM
Data collection: GS
Writing the article: GS, DA, JM
Critical revision of the article: GS, DA, JM
Final approval of the article: GS, DA, JM
Statistical analysis: GS, DA, JM
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Overall responsibility: GS

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DISCUSSION

Dr Vincent Rowe (*Los Angeles, Calif*). The authors' objective was to review and report the charges, case complexity, and use of revascularization among inpatient hospital admissions for diabetic foot ulcers and associated amputations in the United States over the past 10 years. To do so, the authors utilized the inpatient discharge records from the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project. The authors do an excellent job of sorting out such a large volume of information and clearly showed trends in hospital charges, amputation, and complications. With such large databases, there are pros and cons to the information that is accrued; however, the authors clearly point out the shortcomings of this database, and therefore there is no need for me to address those issues. My questions will mainly be focused on the interpretation of their findings.

Over the past decade, patients with diabetic foot ulcers had a shortened length of stay and increased hospital charges. What do the authors attribute to this finding? Is it a reflection of increased healthcare costs, are we driving up the costs with increased endovascular procedures, or are the cases becoming more complex?

Dr Grant H. Skrepnek. Healthcare costs are an important proxy that reflect the intensity of interventions and resources provided in clinical practice. The observation of increased charges with decreased lengths of stay is complex and suggests, at least superficially, an increasing extent of inpatient care that allows patients to be discharged more rapidly. Despite this, the current study's outcomes also reflect other dimensions, including the adoption of medical technologies, evolving standards of care, price inflation, and changes in patient case-mix. In this context, significant increases in the overall case-mix complexity were indeed observed via either the Elixhauser or Deyo-Charlson Comorbidity Index. However, a key limitation in most nationally representative database work involves the lack of specific diabetic foot ulcer (DFU)-related risk factors that capture the degree of ischemia, severity of infection (if present), and other wound characteristics. While either the diffusion of endovascular procedures or the increase in overall case-complexity may indeed explain an observation of increased charges, ceteris parabis, large-scale longitudinal analyses incorporating these disease-specific measures would be helpful in determining the comparative effectiveness of vascular interventions. Finally, although not measured in the current work, the quality of ambulatory care would intuitively be expected to influence the potential outcomes within the hospital setting.

Dr Rowe. Did the authors see any difference in complications and amputations when comparing patients treated in urban large hospitals versus smaller hospitals?

Dr Skrepnek. Empirically, no systematic differences between outcomes based on hospital bed size were observed. A finding that may deserve further investigation, however, involves the observation that lower odds of complications were found in urban (vs rural) hospitals among endovascular procedures: a 57% reduction in the odds of complications for cases involving above-ankle amputations (OR, 0.43; 95% CI, 0.25-0.74; $P = .002$), and a 32% reduction involving cases with no amputation (OR, 0.68; 95% CI, 0.49-0.94; $P = .018$). While higher charges were often associated with urban hospitals, this was not necessarily observed across all procedure types or amputation status.

Dr Rowe. Focusing on amputations, the authors state that the amputation rates are flattening? This is an intriguing issue, as there are so many factors that can contribute to this clinical finding. Do the authors think that the rise in endovascular procedures and minor interventions in an indicator or marker of increased physician awareness of the need for specialty (vascular) care of this diabetic population?

Dr Skrepnek. While the number of inpatient cases involving diabetes has increased from 2001 to 2010, the percentage of those with DFUs has remained constant, slightly below 4%. Also unchanged through the decade, approximately 17% of inpatient DFU cases involved amputations, 9% of DFU cases involve a revascularization procedure, and 24% of revascularized DFU cases involved an amputation. Despite these observations, an increase in minor amputations occurred (from 8% to 12% of DFU cases during the decade), with no change in major above-ankle amputations (9%-10% of DFU cases). The association between these latter outcomes and an increase in endovascular interventions (from under 5% of DFU cases to almost 15%) is compelling. While we support, at least anecdotally, that an increased clinical awareness surrounding the care of the diabetic foot has occurred, we also assert that insufficient resources still remain concerning prevention. Overall, estimates of the economic and clinical burden of illness associated with DFUs should seek to increase awareness of the condition, to enhance comparative and cost-effectiveness analyses of treatment options, and to catalyze the prioritization of clinical and research efforts to improve prevention and cure.

Dr Rowe. Thank you, Society, for selecting me to review this interesting manuscript.

Dr Skrepnek. The authors are also appreciative of the thoughtful and engaging evaluation of this work.